

Review Article

Management of Coronavirus Infection during Pregnancy and Puerperium

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Abstract

Coronavirus infection (COVID-19) has spread rapidly all over the world and turned into a pandemic. Rapid spreading, human-to-human transmission, lack of any definitive treatment, and fatality associated with this disease have a significant impact on public health, making it difficult to control. No increased sensitivity to COVID-19 has been reported in pregnant women compared to the general population. However, pregnant women are more susceptible to diseases than those who are not pregnant, and morbidity and mortality rates are higher. Pregnancy and postpartum management of suspicious or infected pregnancies should be performed by a competent team in this regard due to the high mortality rates associated with similar viruses, SARS-CoV and MERS-CoV infections, in pregnant women. The mortality rate due to SARS-CoV infection is about 25%. There is limited information about COVID-19 infection in pregnant women, and for the time being, treatment management is similar to that in non-pregnant women. Some pregnant patients have fetal distress and preterm labor. There is no evidence that coronavirus can spread from mother to baby. Nevertheless, on February 6, 2020, the SARS-CoV 2 test was found to be positive 36 hours after delivery in the newborn of a woman who was COVID-19 positive. In line with all this information, necessary measures should be taken to prevent contamination in pregnant and puerperal women, and appropriate treatment method should be applied.

Keywords: Pregnancy; Birth; Covid-19; Puerperium ; Medicament

Introduction

This disease, occurring due to Coronavirus infection, spread to the world from the city of Wuhan, China in late 2019. The World Health Organization (WHO) described the virus, which caused the disease COVID-19 as “Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)” in February 2020. According to WHO data, as of 06-11-2020, the total number of reported cases worldwide is 48 534 508 and the number of deaths is 1 231 017(WHO,2020).In the last 20 years, two different corona viruses have caused severe disease in humans; “Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV)” and “Middle East Respiratory Syndrome Coronavirus (MERS-CoV)”.SARS emerged in February 2003 and led to 8.000 infected cases and 770 deaths(Hui and Zumla,2019).Mortality rate was reported as 25%

in pregnant women(Wong et al.,2004).MERS occurred in 2013, causing 860 deaths in 2.500 cases(Rasmussen et al., 2020).Mortality rate in pregnant women was reported as 23%.Mortality rate of Covid 19 varies between 3 and 4% (WHO,Situation Report,2020).SARS-CoV-2 has a genetic similarity of 79% with SARS-CoV and 50% with MERS-CoV(Lu et al., 2020).The virus is spread by coughing and sneezing from sick individuals. It can be transmitted through scattered droplets and contaminated surfaces by touching the eye, mouth and nasal mucosa with hand. As a result of the investigations regarding the fecal-oral transmission of COVID-19, it is known that the nucleic acid belonging to the virus is detected in the feces, but there is no data about contagion (Turkish Medical Association, Covid-19,2020). It is known that the droplet usually does not travel further than 2 meters.

Contamination has also been reported from asymptomatic individuals (Republic of Turkey Ministry of Health, 2020). Incubation period varies from 0 to 24 days (Guan et al., 2020). In one study, viral transmission from oropharyngeal samples was reported to occur during approximately for 20 days (8-37 days) (WHO-China Joint Mission on Coronavirus Disease 2019, 2020).

Common symptoms of the infection include fever, cough, dyspnea, and fatigue. Less common symptoms are pain and ache, sore throat, diarrhea, conjunctivitis, headache, loss of taste or smell, skin rash or discoloration of the fingers or toes (WHO, 2020). In severe cases, pneumonia, severe acute respiratory infection, renal failure and even death may develop. Diagnosis in suspected cases is made with quantitative reverse transcription-polymerase chain reaction (qRT-

PCR) analysis of samples obtained from lower and/or upper airways. In cases of high suspicion, the test is repeated in cases where the first test is negative. If the second quantitative reverse transcription polymerase chain reaction analysis is also negative, COVID-19 is excluded (Republic of Turkey Ministry of Health, 2020).

In cases diagnosed with COVID-19, ground-glass opacities, which are typical findings in Computed Tomography (CT), were observed in 56.4% of the patients. In 17.9% of non-severe cases, no radiological findings were observed (Turkey Maternal Fetal Medicine and Perinatology Association (TMFTP), 2020). Typical findings can also be seen by ultrasound in COVID-19 cases (Opinion of the Turkish Perinatology Association, 2020).

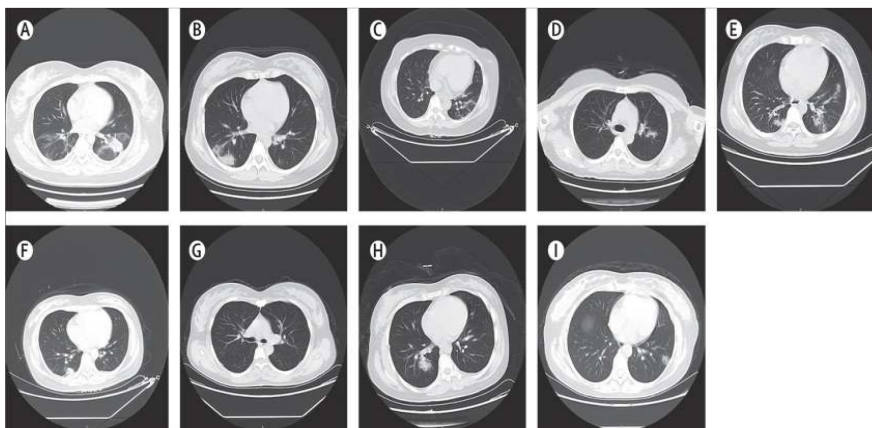


Figure 1. Ground glass opacities in CT scans of nine patients (Huijun Chen ph.D, Juanjuangou MS, 2020, LANCET)

In normal lung examination, a pleural line that echoes regularly under the costae is observed, and just below it are lines of reverberating artifact (lines A). Small subpleural consolidations, white lung areas and vertical artifacts (B-lines) are observed bilaterally in the anterior and posterior hemithorax in lung ultrasound examinations performed in COVID-19 cases.

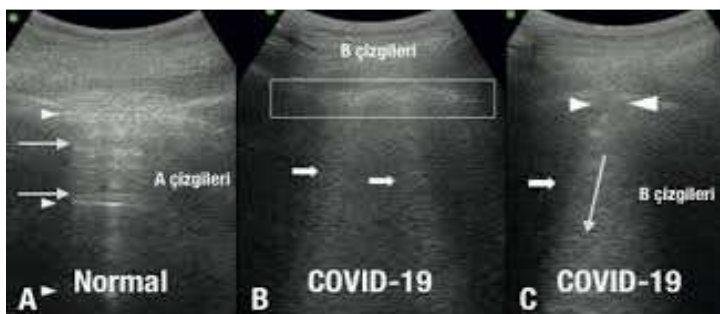


Figure 2. Maternal-Fetal Medicine and Perinatology Society of Turkey

A: Transverse artifacts observed in normal lungs (A lines)

B and C: In COVID-19 cases, irregular pleural thickening in the lung and vertical artifacts that radially extend downward (B lines)

The mortality rate of COVID-19 may differ depending on the changes that could emerge in the genetic structure of the virus. There is no vaccine or antiviral treatment for the disease yet (WHO Director-General's opening remarks at the media briefing on COVID-19, 2020). Antibacterials other than Azithromycin are discontinued in patients who have been diagnosed with COVID-19, unless there is clinical or laboratory evidence of the presence of an additional bacterial pathogen. Oseltamivir and Hydroxychloroquine are added to the treatment in patients with viral pneumonia. Treatment options are defined as Lopinavir/Ritonavir and ribavirin in patients with severe pneumonia that did not respond to the first treatment (Tirmikcioglu, 2020). The Ministry of Health of the Republic of Turkey recommends initiating Hydroxychloroquine treatment immediately in symptomatic patients who are assumed to have the possibility of COVID-19. The combined use of possible treatment options in COVID-19 patients should be considered by evaluating all patient-based findings and available literature. However, there is no clear data on the use of drugs used in treatment in pregnant women with the diagnosis of COVID-19. Hydroxychloroquine has been used in the treatment of malaria and rheumatologic diseases in pregnant women and no significant adverse effects have been reported with this treatment (Centers for Disease Control and prevention (CDC), Treatment of Malaria: Guidelines For Clinicians, 2020). It should be noted that there is a risk of prolonging the Q-T interval with the use of Hydroxychloroquine and Azithromycin. This can create a risk of death due to arrhythmia. There is no clear information showing that

pregnant women are more sensitive to COVID-19 than non-pregnant women (Tirmikcioglu, 2020). In the retrospective study of Chen et al, which included 9 pregnant women with COVID-19, clinical findings were similar to those who were not pregnant. Fever was reported in seven cases, cough in four cases, pain in three cases, and sore throat and weakness in two cases. Lymphopenia was present in five cases and aminotransferase was elevated in three cases. All cases developed pneumonia but there was no need for mechanical ventilation (Chen et al., 2020). In a retrospective review conducted by Zhu et al, six of nine 9 pregnant women, one of whom had twin pregnancy, developed intrauterine fetal distress, while six had premature delivery (Zhu et al., 2020). It is believed that the disease does not have a vertical transmission (Rasmussen et al., 2020). However, in a recent publication, a neonate born to a mother with COVID-19 had SARS-COV-2 IgM, which raised doubts about the transmission of the disease from mother to baby during pregnancy (Dong L et al, 2020). In a systematic review by Mullins et al, 7 (22%) of 32 pregnant women diagnosed with COVID-19 were asymptomatic. Two cases (6%) received intensive care support while one of them was reported to undergo extracorporeal membrane oxygenation. There was no maternal death. Twenty seven of the cases were delivered by caesarean section and two by vaginal route. While preterm delivery occurred in 15 cases (47%), intrauterine fetal death was encountered in one case and neonatal death in one case. No vertical transmission was detected in 25 cases in the study. The other 3 pregnancies are still ongoing (Mullins et al., 2020). According to WHO, pregnant women do not appear to be at risk of serious disease. In a study of 147 pregnant women, 8% of pregnant women were seriously ill, while 1% were in critical condition (WHO-China Joint Mission on Coronavirus Disease 2019, 2020).

Table1. Collective presentation of COVID-19 and pregnancy-related research and other research findings in the article;

Name of the researcher	Place and year of the study	Study type	Number of the cases	Findings of the pregnant with COVID-19	Need for mechanical ventilation	Intensive care support given to the pregnant	Maternal mortality	Fetal findings	Route of delivery	Presence of virus in the newborn
Chen et al.	Wuhan, China Jan 20 – Jan 31 2020	Retrospectively reviewed	N = 9	Pneumonia (N=9)	n = 0	n = 0	Intrauterine fetal distress (n=6) Preterm delivery (n=6)	n=0
Mullins et al.	England London17, Mar,2020	Systematic review	N= 32	Asymptomatic (n=7, 22%)	n=2 (6%)	n = 0	Cesarean delivery (n=27) Vaginal delivery (n=2)	n=25
Zhu et al	Wuhan, China, 01.01. 2020- 05.01.2020	Retrospectively reviewed	N=10	Fever (N=10) Cough (N=10) Diarrhea (n=1)	n=0	Intrauterine fetal distress (n=6) Preterm delivery (n=5)	n=2
Liu et al	Guangdong,China, 5, May,2020	Retrospectively reviewed	N=13	Fever (n=10) Dyspnea (n=3) MODS (n= 6)	n=6	n=6	n=0	Intrauterine fetal distress (n=5) Preterm delivery (n=6)	Cesarean delivery (n=10)	n=1
Lian Chen, Qin Li	China, Wuhan December 8, 2019, to March 20, 2020,	N=118	Fever (n=84) Cough (n=82) Dyspnea (n=8) Diarrhea (n=8) Asymptomatic (n=6)	n=1	n=7	n=0	Miscarriage (n=7)	Cesarean delivery (n=63)

COVID-19 and Use of Drugs in Pregnancy

Use of Oseltamivir: Vera Ehrenstein and her colleagues examined the relationship between the use of oseltamivir in pregnancy and the outcomes of pregnancy in an article published in 2018. The association with congenital heart defects was present for etiologically implausible exposure periods and for known safe exposures. There is no evidence of association between prenatal exposure to Oseltamivir and any other pregnancy outcomes (Ehrenstein et al., 2018). In their cohort study, Christina D. Chambers et al. compared the data such as major birth defects, spontaneous abortion, preterm birth in pregnant women treated or not treated with oseltamivir, and they found no evidence of increased risk with use of Oseltamivir. These data on Oseltamivir are reassuring for pregnant women who need to be treated for infection or post-exposure prophylaxis (Chambers et al., 2019). Case reports do not offer any causality in terms of congenital anomalies. According to the 2018 report of the manufacturer Roche, in which pregnancy records based on voluntary notification are evaluated, Oseltamivir does not have an adverse effect on pregnancy. However, in voluntary reports, it is not sufficient to measure the effect of the drug in pregnancy; because there is no information on oseltamivir exposures that have not been reported (Wollenhaupt et al., 2014). In 2019, Carla M. Van Bennekom and colleagues conducted a study to investigate the relationships between Oseltamivir and specific birth defects. Largely null findings for specific defects are reassuring. The association with intestinal malrotation, while unstable, warrants further investigation (Bennekom et al., 2019).

Use of Hydroxychloroquine: Hydroxychloroquine have a long-standing history in the prevention and treatment of malaria and the treatment of chronic inflammatory diseases including Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA) (Sanders et al., 2020). These agents also have immunomodulatory effects by diminishing cytokine production and inhibition of autophagy and lysosomal activity in host cells (Zhou et al., 2020; Devaux et al., 2020). In 2016, the European Rheumatism Association (EULAR) report on the use of anti-rheumatic drug in pregnancy indicated that Hydroxychloroquine treatment did

not increase the risk of congenital malformation according to existing evidence. It was suggested that this drug can be continued for disease exacerbation or maintenance of remission during pregnancy (Skorpen et al., 2016). There is no high-quality evidence for the efficacy of Chloroquine/Hydroxychloroquine treatment of SARS or MERS. In a news briefing from China, Chloroquine has been reported to successfully result in improvement of radiological findings, enhanced viral clearance and decreased disease progression during treatment of over 100 COVID-19 cases (Gao et al., 2020). The dosage of Chloroquine for treatment of COVID-19 is 500 mg orally once or twice a day (Colson et al., 2020) (National Health Commission and State Administration of Traditional Chinese Medicine, 2020). A physiologically based pharmacokinetic modeling study recommended an optimal dosage regimen of 400 mg A loading dose of 400 mg twice daily of Hydroxychloroquine given orally, followed by a maintenance dose of 200 mg given twice daily (Yao et al., 2020) Hydroxychloroquine is also recommended for malaria prophylaxis in pregnant women who have to travel to endemic regions. Hydroxychloroquine is considered safe in compulsory situations since malaria, which has a rather severe course due to decreased cellular responses during pregnancy, is thought to cause much more harm to pregnancy (CDC, Yellow Book, 2019)

Use of Azithromycin: According to a randomized controlled study conducted by Oriyomi Akinyotu et al. in 2019, use of Azithromycin is safe in malaria and Human Immunodeficiency Virus (HIV) infections (Akinyotu et al., 2019) in their studies, Manuel Krone et al. stated that Azithromycin is an appropriate antibiotic for invasive meningococcal disease and post-exposure prophylaxis. Azithromycin is approved for both adults and children and can even be used during pregnancy. Owing to easier administration and lower toxicity, it may be an alternative to rifampicin and ciprofloxacin (Krone et al., 2020). In a study investigating the relationship between antibiotic use and spontaneous abortion during pregnancy in 2017, it was reported that the use of Azithromycin may be associated with miscarriages (Muanda et al., 2017).

Use of lopinavir/ritonavir: Early reports of Lopinavir/Ritonavirin for the treatment of COVID-19 mostly consist of case reports and minor retrospective, non-randomized cohort studies, making it difficult to detect the direct treatment effect of Lopinavir/Ritonavir (Yao et al., 2020). More recently, Cao et al. analyzed the results of open-label, randomized controlled trial (RCT) that compared the effectiveness of Lopinavir/Ritonavir with standard management in 199 COVID-19 patients; The available data show that Lopinavir/Ritonavir plays a limited role in the treatment of COVID-19 (Cao et al., 2020). According to thousands of pregnancy data received until 2019, the rate of congenital malformation in pregnant women receiving Lopinavir for HIV is around 2.1% and is similar to that of the general population (Antiretroviral Pregnancy Registry Steering Committee, 2019).

Use of ribavirin: Ribavirin was often used in combination with interferon in the treatment of MERS with no significant effect on clinical outcomes or viral clearance. The scarcity of clinical data regarding ribavirin for treatment of SARS-CoV-2 implies that its therapeutic role is not known precisely (Arabi et al., 2020). In a large MERS observation study, safety concerns regarding severe dose-related hematological toxicity have been observed, approximately 40% of patients receiving ribavirin and interferon require blood transfusion (Arabi et al., 2020). Ribavirin is also a known teratogen and contraindicated in pregnancy (CDC, Interim Clinical Guidance, 2020). It has been found that 7 of 85 neonates born to pregnant women who received ribavirin and gave live births had congenital defects and these defects were not similar (Sinclair et al., 2017).

ANTIVIRAL TREATMENT RECOMMENDATIONS IN PROBABLE/DEFINITIVE COVID-19 CASES		
Name of the medication	Daily Adult Dose, Route of Administration	Duration of treatment (days)
Primary Treatment Regardless of the Clinical Severity of the Disease		
<i>Treatment in Definitively Diagnosed COVID-19 Cases with Fever</i>		
Oseltamivir tab, 75 mg +	2×75 mg, oral	5 days
Hydroxychloroquine, 200 mg tab	2×400 mg loading dose Followed by 2×200 mg tablet, oral	5 days
<i>Treatment in Possible/Definitive Diagnosed Patients with Pneumonia</i>		
Oseltamivir tab, 75 mg +	2×75 mg, oral	5 days
Hydroxychloroquine, 200 mg tab	2×400 mg loading dose Followed by 2×200 mg tablet, oral	5 days
<i>According to the Physician's Decision</i>		
In addition to above + Azithromycin	500mg tab on first day, followed by oral 250mg/day for 4 days	5 days
<i>Treatment in Severe Patients Who Do not Respond to the First Treatment</i>		
Favipravir 200 mg tablet or	2×1600 mg loading	5 days
Lopinavir 200mg/Ritonavir 50 mg tablet	2×600 mg maintenance 2×2 tablet oral	10-14 days

Routine Pregnancy Check-ups in COVID-19 Pandemic: Obstetrics and Gynecology departments should prepare a room for the first admittance of potential cases. This room should be right next to the entrance and an arrangement should be made so that spread of the virus to other patients is prevented. The waiting area for the relatives of suspected patient should be set away from

the other waiting areas. The personnel working in this section should be designated in advance. An appropriate space should be ready for the personnel who will be performing examination next to this room, to wear the necessary protective equipment. Health personnel should use gloves, isolation gown, goggles/face protection, and a medical mask for the above mentioned physical

examination and care of the suspected/patient. An isolated negative pressure room should be prepared and protective equipment should be worn and removed in a room with direct access to this room. In the delivery room, an isolated, negative pressure (if possible) room and a surgery room for cesarean section operations should be prepared (TMFTP, 2020).

Routine prenatal care of pregnant women without risk is necessary and should be planned. In asymptomatic patients, the first three months of ultrasound screening and detailed ultrasound evaluation between 18-22 weeks should be performed as much as possible (TMFTP, 2020).

Pregnant women with suspected COVID-19 infection and those with definitive diagnosis but remaining asymptomatic or exhibiting mild findings should be monitored every 2-4 weeks in terms of fetal growth and amniotic fluid volume assessment (Favre et al., 2020). Excessive ultrasonographic examinations should not be performed in high-risk pregnant women unless the fetal condition requires otherwise.

The gynecologist and obstetrician should decide the frequency of ultrasonographic examinations based on the condition of the mother and fetus (TMFTP, 2020).

If the pregnant woman with suspected contact COVID-19 is not required to be hospitalized for any other reason, she is asked to stay at home as much as possible and stay away from public areas for 14 days.

In cases where it is necessary to go to public areas, it is requested to wear a medical mask. It is recommended not to accept visitors to the house, to ventilate the room well, to be as separate from other members of the household as possible, to use different towels, different crockery and kitchen utensils and to eat meals at different times (Republic of Turkey Ministry of Health, 2020-Royal college of obstetricians & gynaecologists, 2020).

Suspected or diagnosed cases should be followed up in an appropriate hospital setting. These cases should be observed in isolated rooms with negative pressure. If the hospital has a heavy workload and there is no appropriate conditions for hospitalization, it may be considered to follow-up the diagnosed pregnant women with mild symptoms at home rather than hospital follow-up. After recovery of suspected or diagnosed asymptomatic and mild cases, fetal growth and amniotic fluid volume should be monitored every 2-4 weeks with Doppler, if necessary (Royal college of obstetricians & gynaecologists, 2020).

Isolation and follow-up of pregnant women with suspected COVID-19;

- Pregnant women with mild clinical complaints may not initially be hospitalized, and strict observation at home may be considered. (Centers for Disease Control, 2020)
- Suspected cases should be isolated and treated in the hospital. Definitely diagnosed cases should be treated in a negative pressure isolation chamber (Centers for Disease Control, Interim Clinical Guidance, 2020).
- A special negative pressure operating room and neonatal isolation room should be prepared in designated hospitals. All medical personnel involved in caring for cases of definitive COVID-19 infection should wear masks, goggles, face shields, surgical gowns, and gloves (Centers for Disease Control, Interim Clinical Guidance, 2020).
- A definitely diagnosed patient who is severely ill should be taken to a negative pressure isolation room in the intensive care unit (Centers for Disease Control, Interim Clinical Guidance, 2020)
- If negative pressure isolation chambers are not available, patients should be isolated in single rooms or grouped together in the same room, with a distance between them after confirming the COVID-19 infection (Centers for Disease Control, Interim Clinical Guidance, 2020).

Maternal monitoring in suspected COVID-19 cases;

- Vital signs and oxygen saturation level are closely and carefully monitored to minimize maternal hypoxia.
- Arterial blood gas analysis is done,
- Images of lungs are repeatedly obtained if necessary,
- Complete blood count, kidney and liver function tests and clotting tests are regularly evaluated (Opinion of the Turkish Perinatology Association, 2020).

Fetal follow-up in suspected COVID-19 cases;

- On 26-28th weeks of gestation, cardiotocography and ultrasound evaluation of fetal growth and amniotic fluid volume are performed with umbilical artery Doppler for fetal heart rate monitoring.
- Monitoring devices and ultrasound equipment should be disinfected before and after use (Opinion of the Turkish Perinatology Association, 2020).

Prenatal follow-up in suspected COVID-19 cases;

Regardless of the time of the infection, pregnancy should be monitored according to clinical and ultrasound findings. All examinations for obstetric emergencies should be carried out in accordance with current guidelines. All routine appointments should be delayed for 14 days or until test results are positive or two consecutive test results are negative (Boseley, S., 2020).

Non-severe disease follow-up of cases with definitive COVID-19;

- Fluid and electrolyte balance should be maintained; symptomatic treatment and follow-up are the same as for suspected cases.
- Currently, there is no proven antiviral therapy for COVID-19 patients, but antiretroviral drugs are being therapeutically tried in patients with severe symptoms. If antiviral therapy is to be considered, this

should be done after carefully discussing with virologists; pregnant patients should be well informed about the possible side effects of antiviral therapy for the patient and the risk of fetal growth restriction.

- When definitive diagnosis is made for secondary bacterial infection, blood culture, medium or catheterized urine samples should be taken, and microscopic and culture monitoring should be performed. Bacterial infection should be treated with appropriate antibiotics in a timely manner. Empirical or inappropriate use of antibiotics should be avoided when there is no clear evidence of secondary bacterial infection.

- Fetal monitoring: On 26-28th weeks of pregnancy, cardiotocography for fetal heart rate and ultrasound assessment of the volume of amniotic fluid with umbilical artery with Doppler should be performed when necessary (NIH clinical trial of Remdesivir to treat COVID-19 begins, 2020 - Republic of Turkey Ministry of Health, 2020).

Severe and critical disease follow-up of cases with definitive COVID-19;

- The severity of COVID-19 pneumonia is defined by the pneumonia guidelines of various medical associations (Metlay et al., 2019). Severe pneumonia is associated with a high maternal and perinatal mortality rate, so persistent treatment, including hydration, oxygen therapy, and chest physiotherapy and supportive measures are required. The case should be monitored in the negative pressure isolation room in the intensive care unit by a multidisciplinary team including obstetrician, perinatologist, intensive care specialist, obstetric anesthesiologist, midwife, virologist, microbiologist, neonatologist and infectious diseases specialist. Pregnant women should lie down preferably in the left lateral position (Plante et al., 2019).

- Antibacterial therapy: When there is a suspicious or confirmed secondary bacterial infection, after discussing with microbiologists, appropriate antibiotic

therapy should be applied immediately with antiviral therapy (Plante et al., 2019).

- Blood pressure monitoring and fluid balance management: Conservative fluid management measures should be taken in patients without septic shock; In patients with septic shock, fluid resuscitation and inotropes are required to maintain the mean blood pressure of 60 mmHg and lactate level <2 mmol/L (Plante et al., 2019).
- Oxygen Therapy: Additional oxygen ($\geq 95\%$) should be used to maintain oxygen saturation; Oxygen should be given immediately to patients who develop hypoxemia and/or shock, and ventilation should be performed under the guidance of the intensive care specialist and obstetric anesthetists according to the condition of the patient (Opinion of the Turkish Perinatology Association, 2020).
- Fetal Monitoring: When the patient is stabilized, preferably on 26-28th week of pregnancy, cardiotocography should be performed for fetal heart rate monitoring and, if necessary, an ultrasound assessment of fetal growth and amniotic fluid volume with the umbilical artery Doppler (Opinion of the Turkish Perinatology Association, 2020).
- Timing the delivery: Time of the delivery should be evaluated on a case-by-case basis by the multidisciplinary team (Opinion of the Turkish Perinatology Association, 2020).
- Vaccine or Antiviral therapy: There is no vaccine or antiviral therapy for this disease yet (WHO Director-General's opening remarks at the media briefing on COVID-19, 2020).

There are studies on drugs such as Remdesivir, Hydroxychloroquine, Lopinavir-Ritonavir, Tocilizumab in the treatment. The Ministry of Health of the Republic of Turkey recommends the use of Hydroxychloroquine, Oseltamivir and Azithromycin, according to the algorithm announced (Republic of Turkey Ministry of Health, 2020).

Intensive care approach in pregnancy; COVID-19 in pregnant women can also be manifested by severe respiratory tract infection (severe pneumonia), acute respiratory distress syndrome (ARDS), sepsis, septic shock, myocarditis, arrhythmia and cardiogenic shock, and multiple organ failure tables. These patients should be monitored in the intensive care unit. When intensive care and cardiopulmonary resuscitation are required in pregnant women, physiological changes during pregnancy should be prioritized (TMFTP, 2020).

Intrapartum management;

If the labor has already started, cases should be monitored in the isolated unit in negative pressure isolated rooms in the conditions declared by the Turkish Ministry of Health. The points to be considered in monitoring include;

- Maternal fever, oxygen saturation in the blood, respiratory rate, pulse, and blood pressure should be closely monitored (TMFTP, 2020).
- Fetus should be monitored with continuous electronic fetal monitoring (TMFTP, 2020).
- Blood Oxygen saturation should be kept $\geq 95\%$ (TMFTP, 2020).
- There is no clear recommendation regarding the mode of delivery. Deliveries were mostly done by cesarean section. It is thought that respiratory distress in pregnant women plays a role in the high rates of cesarean section. There is no evidence that vaginal secretion creates a risk of transmission to the baby during vaginal delivery (TMFTP, 2020).
- There is no evidence that a suspected or definitive COVID-19 pregnant woman cannot receive an epidural or spinal block. Regional anesthesia should be preferred for vaginal delivery and cesarean section. However, the use of Entonox has no effect on virus spread, it should be used with a microbiological filter (TMTF, 2020).

- If the patient's condition worsens, the transition from vaginal delivery to cesarean delivery should be considered (TMFTP, 2020).
- In respiratory distress worsens and fever rises or fatigue develops during vaginal delivery, an attempt should be done to shorten the 2nd stage of delivery (TMFTP, 2020)
- There is no clear information about the superiority of early or late cord clamping (TMFTP, 2020).
- Fluid balance should be carefully monitored, excess fluid should be avoided (TMFTP, 2020).

Management of postnatal period;

All newborns should be tested for COVID-19. Some reports from China suggested that those with confirmed COVID-19 should be separated from their babies for 14 days. However, this may have negative effects on mother bonding and nutrition. In this respect, it is recommended to keep the mother and baby together. This situation should be decided by the multidisciplinary team according to the benefit-loss balance (Royal college of obstetricians & gynaecologists, 2020).

Breast-feeding

There is insufficient evidence for the safety of breastfeeding and the need for mother/infant separation (Yang et al., 2020).

- Separation of newborn from mother is considered the best option in the presence of severe infection in the mother, but breast milking can be continued to maintain lactation (Yang et al., 2020).
- Precautions should be taken to clean the breast pumps (Yang et al., 2020).
- If the patient is asymptomatic or slightly affected, breastfeeding can be considered in line with the decisions and measures taken by the mother and healthcare providers together; sometimes separation may not be

possible in places with limited facilities (Yang et al., 2020).

- The main concern is that the virus is more likely to be transmitted by droplets than breast milk; therefore nursing mothers should wash their hands and wear a three-layer surgical mask before touching their baby (Yang et al., 2020).
- In the case of staying together in the room, the baby cot should be kept at least 2 meters from the maternal bed, and a curtain-like physical barrier may be used (European Centre for Disease Prevention and Control, 2020). Lactation inhibition can result from inability of mothers with COVID-19 infection to breastfeed their babies directly or from the necessity to separate newborn from mother (Royal college of obstetricians & gynaecologists, 2020).

In this review, we identified the problems of coronavirus infection associated with pregnancy and postpartum period. We have compiled up-to-date information on what to do about problems of pregnant and puerperal women related to COVID-19 with regard to healthcare professionals. In the light of this information, the healthcare personnel should pay attention to the necessary recommendations on issues such as obeying the social distance and hygiene rules, using protective equipment, breastfeeding, and applying the medicines ordered by the physician, for protection and treatment of pregnant and puerperal women in terms of COVID-19 disease.

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